

Appl. No. 10/087,473 (Docket 090/003)
Amdt. dated May 10, 2006
Reply to Office Action of February 10, 2006

REMARKS/ARGUMENTS:

Applicants have canceled claims 2, 3, and 7-30 without prejudice or disclaimer. Applicants reserve the right to reintroduce the subject matter of that claim at a later point in prosecution. Applicants amended claim 1. Claims 1, 4-6, and 31-32 are currently pending in this application. Reconsideration and allowance of the application is respectfully requested.

Double Patenting

The Office provisionally rejected claims 1, 4-6, and 30-32 on the grounds of nonstatutory obviousness-type double patenting over claims 34-46 of U.S. Application Serial No. 09/888,309. The '309 application has been abandoned, and thus the rejection is moot.

Rejection under 35 U.S.C. §112, first paragraph (enablement) of claims

The Office rejected claims 1, 4-6, and 30-32 under 35 U.S.C. §112, first paragraph, as allegedly not being enabled by the specification. Action at page 4. The Office argued that the "working examples in the specification provide guidance with regard to using specific TGF- β superfamily antagonists, noggin and follistatin" and contended that "it would not be predictable to use any particular antagonist, other [than] the exemplified noggin and follistatin, in order to produce neuron[s] that express TH." *Id.* at page 6-7.

Applicants traverse this basis for the rejections and disagree with the Office's contentions. However, without acquiescing in the Office's rejection and solely to facilitate the prosecution of this application, Applicants have amended claim 1 so that it now is directed to the use of noggin and/or follistatin to produce a population of cells comprising neurons that express tyrosine hydroxylase. Thus, Applicants request reconsideration and withdrawal of the enablement rejection.

Rejection under 35 U.S.C. §103(a)

The Office rejected claims 1, 4-6, and 30-32 under 35 U.S.C. §103(a) as allegedly being obvious over Thomson in view of Weiss and in further view of Melton.

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In making its assertions of obviousness, the Office pointed to three references to allegedly find the various limitations of the claims. However, in order to properly make its *prima facie* case, the Office must also present reasonable and supported arguments that one skilled in the art prior to the filing would have been motivated to combine the teachings of those references and would have reasonably expected that combination to work. Mere conclusory hand-waving is not sufficient.

For example, the various experiments in the Melton reference involve *in vivo* experiments in a frog model. The Office has not asserted that those experiments involved embryonic stem cells in any way. Thus, the Office must explain why one skilled in the art would have thought to take the teachings of Melton regarding *in vivo* frog experiments and apply them to the *in vitro* differentiation of human embryonic stem cells. In addition, the Office must also explain why the skilled artisan, based on the teachings of Melton, would have reasonably expected noggin and/or follistatin to promote the *in vitro* differentiation of human embryonic stem cells to neurons that express tyrosine hydroxylase. Applicants note that the Examiner has not even pointed to any disclosure in Melton teaching that the use of follistatin can generate TH-expressing neurons (as required by the current claims). That is not all, however. The Office must also explain why one skilled in the art would have been motivated to further combine the teachings of Weiss, which employ neural stem cells as their starting point.

In other words, when the Office attempts to combine three references with disparate teachings and quite different starting points (hES versus *in vivo* frog versus neural stem cell), the Office bears the burden to provide support for its contention that one skilled in the art would connect those disparate teachings and reasonably expect that combination to work. Here, the Office has done no more than make unsupported, conclusory statements regarding the motivation and expectation of success elements of its rejection. For example, the Office merely states that “[o]ne of ordinary skill in the art would have been motivated to do so because the presence of factors such as follistatin and noggin can be employed to maintain the integrity of a culture of terminally-differentiated neuronal cells by preventing loss of differentiation as taught by Melton . . .” Action at page 10. The Office

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has not explained why that statement has any relevance whatsoever to the question of whether one skilled in the art would have been motivated to combine the teachings of Thomson, Weiss, and Melton to end up with a method of differentiating human embryonic stem cells *in vitro* through use of noggin and/or follistatin to produce neurons that express TH. The Office then concluded without even an attempt at providing any support that there would also be a reasonable expectation of success.

The use of speculation unbounded by fact or reasoning is simply insufficient for meeting the burden of establishing a *prima facie* case. Applicants request that the Office either properly make out a *prima facie* case of obviousness or withdraw the rejection.

Fees Due

Should the Patent Office determine that a further extension of time or any other relief is required for further consideration of this application, Applicants hereby petition for such relief, and authorize the Commissioner to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,

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